

REMARKS/ARGUMENTS

Claims 1-20 are active.

Claims 1-4 have been amended for clarity.

No new matter is believed to have been added.

Applicants acknowledge the finality of the restriction. However, Applicants ask that it be at least reconsidered for Claim 14 and also consider the possibility of rejoinder of Claims 15 to 20 to the elected subject matter upon finding the same allowable. If that finding is applicable, Applicants have taken the opportunity to amend the claims so that they too are ready for allowance.

The rejection under 35 USC 101 is no longer applicable as the claims have been amended as suggested--to include "biologically pure culture."

The rejection under 35 USC 112, second paragraph is no longer applicable as the noted terms have been either deleted or amended consistent with the suggestions in the Action.

The rejection under 35 USC 112, first paragraph relating to the deposit status of *B. choshinesis* HPD31-SP3 is addressed by Applicants avering that the deposited material has been deposited and accepted under the terms of the Budapest Treaty. Applicants further state that all restrictions on the availability of this deposit to the public will be irrevocably removed upon the grant of a patent of the present application.

The rejection under 35 USC 103(a) citing Modest, Frascotti and Matsusaki.

The first assertion underlying the rejection is that the claimed *Brevibacillus choshinensis* is the same or very nearly the same as the *B. brevis* ATCC8185 strain in Modest. However, as apparent from the following, ATCC 8185 strain in Modest is not *B. brevis* but *B. parabrevis*.

Namely, the Modest strain does not fall into the classification of *Brevibacillus choshinensis*.

a) The strain described in Modest et al. is the mutant of ATCC 8185. As is well-known in the field, the ATCC number is identification number of the strain that is invariable even if taxonomic name of the strain is shifted.

b) In the page of ATCC 8185 of ATCC catalogue, it is described that “Organism: *Brevibacillus parabrevis* deposited as *Bacillus brevis* Migula” (see enclosed ATCC catalogue printout of the pages which describe ATCC 8185 (see attached Reference R2-1-  
<http://www.atcc.org/ATCCAdvancedCatalogSearch/ProductDetails/tabid/452/Default.aspx?ATCCNum=8185&Teleplate=bacteria>)).

c) Attached to this filing is a publication by Shida et al (*Anonie Leewenhoek* 70:31-39 (1996)). In Shida et al, ATCC 8185 described in Modest is not *B. brevis* but *B. parabrevis* strain in Table 1 (No. 28). Shida et al also describes that *Brevibacillus choshinensis* and *Bacillus brevis* ATCC 8185 in Modest are quite different. In view of this, the rejection cannot be sustained.

Namely, Shida provides electrophoretic whole-cell protein analysis as a way to distinguish species. As apparent from Figure 1 (upper panel) the protein patterns of *Brevibacillus choshinensis* and *B. brevis* ATCC 8185 are quite different and indeed distinct. A similar set of differences are shown also in FIG. 3 aligned with a dendrogram. Again what this shows quite clearly is that these two organisms are different, see for example, FIG. 3 of the Shida paper and note that the prominent band at about 66 kD in the *B. choshinensis* is completely absent from *B. parabrevis* (and also *B. brevis*). See also the prominent band between the 66 and 97 kD marker in *B. choshinensis* and which is not present in the *B. parabrevis* (and also *B. brevis*).

d) A second publication by Shida et al (Shida II) in *The Journal of Systematic Bacteriology* (vol. 46, No. 4, 1996: pp. 939-946) provides even more evidence that the organism are not the same. For example in FIG. 2 and FIG. 3, a primer that was generated to be complementary to a portion of the 16s rRNA genes from the various organisms shows at least that in the short stretch of nucleotides depicted there are at least two differences.

This is clear structural evidence that the two strains are not the same and as “closely related” is a vague an unknown entity, the reliance on Modest provides no teachings relevant to the claimed invention.

e) Moreover, in addition to Shida I and Shida II discussed above, Logan et al. (2002) *International Journal of Systematic and Evolutionary Microbiology*, 52, 953 966--attached (Reference R2-2)-- also shows differences between *Brevibacillus choshinensis* and ATCC 8185.

In Logan et al, ATCC 8185 falls into classification of *Brevibacillus parabrevis* (Table 1), and ATCC 8185, identified in Table 1, Fig. 2, Fig. 4, etc.

Secondly, as described in Shida II, the *B. subtilis* of Frascotti (U.S. 6,284,490) and Matsuzaki et al and *Brevibacillus choshinensis* of the present application fall into different classifications, namely, the former falls into the classification of the genus *Bacillus* whereas in contrast, the latter falls into the classification of the genus *Brevibacillus*, and, as apparent from Fig. 3 of Shida I and Fig. 1 and Fig. 4 of Shida II, the *B. subtilis* of Frascotti (U.S. 6,284,490) and Matsuzaki; and *Brevibacillus choshinensis* of the present application are not related.

They are located a long distance with respect to each other on a dendrogram (Fig. 1 of Shida II); in particular see Fig. 4 of Shida). There are no resemblances of the species. Moreover, as one piece of structural evidence that *B. subtilis* and *Brevibacillus choshinensis*

are different microorganisms with distinct properties and not related, it can be noted that the *imp* and *emp* genes do not exist in *B. subtilis* but are in *Brevibacillus choshinensis*.

This is clear evidence that structurally the two strains are not related. Therefore, Frascotti and Matsuzaki provide no teachings to what is claimed.

The claimed “*hos*” gene is different from that disclosed in Matsuzaki et al. Both genes differ in base sequence and position. The former is irrelevant to the latter. Matsuzaki et al. does not disclose the claimed “*hos*” gene. They are given the same name accidentally.

a) First of all, Matsuzaki et al. does not disclose any DNA sequence of “*hos*” gene.

b) Matsuzaki et al. only discloses that “*hos*” gene is located between *cysA* -*rpoB* region of the *Bacillus subtilis* chromosome (Fig. 1).

c) In spite that whole information about *Bacillus subtilis* genome can be found in SubtiList (URL: <http://genolist.pasteur.fr/SubtiList>), no “*hos*” gene is located between *cysE* (*cysA*)-*rpoB* region, in SubtiList. See enclosed SubtiList printout which lists all genes between *cysE* and *rpoB* (see attached Reference R1-1- <http://genolist.pasteur.fr/SubtiList/>).

In SubtiList website, as the synonym of *cysA*, *cysE* is used. See enclosed SubtiList printout of the pages which describes *cysE* (see attached Reference R1-2- [http://genolist.pasteur.fr/SubtiList/genome.cgi?gene\\_detail+BG10155](http://genolist.pasteur.fr/SubtiList/genome.cgi?gene_detail+BG10155)).

Therefore, it is clear that *cysA* is *cysE*.

d) Furthermore, Applicants examined the genomic homology between the claimed “*hos*” gene (SEQ ID NO:1) and 13 genes between *cysE* and *rpoB* in *Bacillus subtilis* genome (R1-1, R1-2), there shown no significant homology (see the Table 1 below).

e) The obtained results are shown in the Table 1.

Table 1

	Amino Acid Sequence Homology	DNA Sequence Homology
cysS	8.8%	46.6%
yazC	9.2%	48.7%
yacO	8.5%	48.0%
yacP	13.4%	44.7%
sigh	15.3%	47.8%
rpmGB	14.3%	52.6%
secE	23.1%	48.3%
nusG	8.0%	42.9%
rplK	8.9%	49.2%
rplA	11.8%	45.7%
rplJ	12.7%	49.7%
rplL	13.0%	49.2%
ybxB	15.0%	45.6%

f) As described above, it is quite clear that “*hos*” genes in Matsuzaki et al. and the present application are completely different.

g) All genomic sequence from *cysE* to *rpoB* in *Bacillus subtilis*, 13 genes between *cysE* and *rpoB*, amino acid sequence encoded by each genes are respectively listed in enclosed references (R1-3, R1-4, R1-5).

Reference R1-3: All genomic sequence from *cysE* to *rpoB* in *Bacillus subtilis*

Reference R1-4: 13 genes located in the region between *cysE* and *rpoB*

Reference R1-5: Amino acid sequence encoded by above genes

Also attached are results of homology confirmation by GENETYX as

R1.6: GENETYX: Amino Acid Sequence Homology

R1-7: GENETYX: Nucleotide Sequence Homology

Reconsideration and withdrawal of the rejection is requested.

Respectfully submitted,

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